

AMENDMENT

The following listing of claims replaces all prior listings of claims in this application.

Claims 1-23 (Canceled)

24. (Currently Amended) A device for separating large nucleic acid molecules from small nucleic acid molecules, wherein the large nucleic acid molecules exhibit a first radius of gyration, the device comprising:

a plurality of alternating constricted and unconstricted regions forming a channel and having the nucleic acid molecules disposed therein;

the unconstricted regions having a transverse dimension equal to or greater than the first radius of gyration, and length sufficient to allow the large nucleic acid a-larger molecules to attain approach its their equilibrium shape as ~~[[it]]~~ they move~~[[s]]~~ through the channel in response to a driving force; and

the constricted regions having a transverse dimension ~~sufficiently small~~ substantially smaller than the first radius of gyration, to influence the shape of ~~some of the~~ nucleic acid molecules moving through the channels.

25. (Currently Amended) The device of claim 24, wherein the constricted regions provide a trapping point adjacent an unconstricted region, and wherein the larger molecules have a wider contact area at the trapping point of the constricted regions, and thus have a higher probability of escaping the unconstricted region through a constricted region than ~~[[a]]~~ the smaller molecules.

26. (Currently Amended) The device of claim 24, wherein the nucleic acid molecules in the unconstricted regions are in a relaxed state, and are entropically hindered from entering adjacent constricted regions in the channel.

27. (Original) The device of claim 24, and further comprising a substrate supporting the channel.

28. (Currently Amended) The device of claim 24, wherein the constricted regions are ~~nonfluidic~~ nanofluidic, and the unconstricted regions are obstacle free.

29. (Canceled).

30. (Currently Amended) The device of claim 24, wherein both the large and small molecules ~~need to~~ are deformed from their equilibrium states to enter the constricted region.

31. (Currently Amended) The device of claim 24, wherein the equilibrium shape of the ~~larger~~ large molecules is influenced by the constricted region to a greater extent than the equilibrium shape of ~~[[a]]~~ the smaller molecules.

32. (Currently Amended) A device for separating large nucleic acid molecules from small nucleic acid molecules, the device comprising:

a plurality of alternating constricted and unconstricted regions forming a channel and having the nucleic acid molecules disposed therein;

the unconstricted regions having a depth and length sufficient to allow ~~a larger~~ large nucleic acid molecules to attain ~~approach its~~ their first radius of gyration as ~~[[it]]~~ they move~~[[s]]~~ through the channel in response to a driving force;

the constricted regions having a depth substantially less than a radius of gyration of ~~[[a]]~~ smaller molecule nucleic acid molecules; and

means for applying force to the nucleic acid molecules in the channel.

33. (Currently Amended) The device of claim 32, wherein the constricted regions provide a trapping point adjacent an unconstricted region, and wherein the ~~larger~~ large nucleic acid molecules have a wider contact area at the trapping point of the constricted regions, and thus have a higher probability of escaping the unconstricted region through a constricted region than ~~[[a]]~~ the smaller nucleic acid molecules.

34. (Currently Amended) The device of claim 32, wherein the nucleic acid molecules in the unconstricted regions are in a relaxed state, and are entropically hindered from entering adjacent constricted regions in the channel.

35. (Original) The device of claim 32, and further comprising a substrate supporting the channel.

36. (Currently Amended) The device of claim 32, wherein the constricted regions are ~~nonfluidic~~ nanofluidic, and the unconstricted regions are obstacle free.

37. (Currently Amended) The device of claim 32, wherein the small nucleic acids molecules exhibit an equilibrium spherical shape having ~~of a smaller molecule~~ has a radius of gyration, and wherein the constricted region has a transverse dimension less than such radius of gyration ~~equilibrium spherical shape~~.

38. (Currently Amended) The device of claim 32, wherein both the ~~larger~~ large and ~~smaller~~ small molecules ~~need to be~~ are deformed from their equilibrium states to enter the constricted region.

39. (Currently Amended) A device for separating large nucleic acid molecules from small nucleic acid molecules, the device comprising:

an input reservoir and an output reservoir;

a plurality of alternating constricted and unconstricted regions forming a channel coupled between the input and output reservoir and having the nucleic acid molecules disposed therein;

the unconstricted regions having a depth and length sufficient to allow ~~a larger~~ the large molecules to ~~approach its~~ attain their equilibrium spherical shape as ~~[[it]]~~ they move~~[[s]]~~ through the channel in response to a driving force; and,

the constricted regions having a depth substantially less than an equilibrium spherical shape of ~~[[a]]~~ the small nucleic acid ~~smaller~~ molecules.

40. (Original) The device of claim 39, wherein the input and output reservoirs are positioned to contain a buffer solution with molecules to be separated.

41. (Original) The device of claim 40, and further comprising a first contact positioned within the input reservoir to contact the buffer solution and a second contact positioned within the output reservoir to contact the buffer solution.

42. (Original) The device of claim 39, and further comprising a detector positioned about the channel to detect desired molecules in the channel.

43. (Original) The device of claim 42, wherein the detector comprises an optical microscope.

44. (Currently Amended) A device for separating large nucleic acid molecules from small nucleic acid molecules, the device comprising:

a loading chamber;

a plurality of separation channels coupled to the loading chamber, each separation channel having a plurality of alternating constricted and unconstricted regions and having the nucleic acid molecules disposed therein;

the unconstricted regions having a depth and length sufficient to allow ~~a larger~~ the large nucleic acid molecules to ~~approach its~~ attain their equilibrium spherical shape as ~~[[it]]~~ they move~~[[s]]~~ through the separation channel in response to a driving force; and,

the constricted regions having a depth substantially less than an equilibrium spherical shape of [[a]] the small nucleic acid ~~smaller~~ molecules.

45. (Original) The device of claim 44, wherein different separation channels have different structural parameters selected from the group consisting of a transverse dimension and length of each of the regions.

46. (Original) The device of claim 45, wherein the parameters are optimized for the separation of different length ranges of molecules.

47. (Original) The device of claim 44, wherein the loading chamber comprises multiple support pillars.

48. (Original) The device of claim 44, wherein the loading chamber is coupled to a loading channel by an entropic barrier.

49. (Original) The device of claim 44, wherein the loading chamber is coupled to a first electrical contact through an entropic barrier.

50. (Original) The device of claim 49, wherein the separation channels are coupled to a second electrical contact, and wherein the first and second electrical contacts provide an electric field for driving molecules through the separation channels when coupled to a power source.

51. (Currently Amended) A device for separating ~~larger~~ large nucleic acid molecules from ~~smaller~~ small nucleic acid molecules, the device comprising:

a channel having the nucleic acid molecules disposed therein and a depth and length sufficient to allow the large ~~larger~~ nucleic acid molecules to ~~approach~~ attain their equilibrium spherical shape; and

means for creating a series of entropic barriers to selected nucleic acid molecules in the channel.

52. (Original) The device of claim 51, and further comprising means for driving the molecules through the channel.

53. (Currently Amended) A device for separating nucleic acid molecules, the device comprising:
a ~~sequence of an~~ plurality of alternating unconstricted region and an entropic barrier forming a channel and having the nucleic acid molecules disposed therein;

the unconstricted region having a transverse dimension and length sufficient to allow selected nucleic acid molecules to ~~approach~~ attain their equilibrium shape as they move through the channel in response to a driving force; and,

the entropic barrier influencing the shape of selected nucleic acid molecules as they move through the channel.

54. (Original) The device of claim 53, wherein the entropic barrier provides a differential delay of molecules moving through the channel based on the size of the molecules.

55. (Original) The device of claim 53, and further comprising further alternating unconstricted regions and entropic barriers forming the channel.

56. (Canceled)